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10/541,947	12/12/2005	James N. Petite	297/204 PCT/US	1436

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EXAMINER
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WILSON, MICHAEL C

ART UNIT	PAPER NUMBER
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1632

MAIL DATE	DELIVERY MODE
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04/10/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/541,947	PETITTE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Michael C. Wilson	1632	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 07 January 2008.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-4, 6-10 and 12-57 is/are pending in the application.
- 4a) Of the above claim(s) 12-57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-4 and 6-10 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |                                                                                        |                                                                   |
|----------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                       | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____.                                     |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>1-7-08</u> .                                                  | 6) <input type="checkbox"/> Other: _____.                         |

### **DETAILED ACTION**

Claims 5 and 11 have been canceled. 1-4, 6-10 and 12-57 remain pending.

Applicant's arguments filed 1-7-08 have been fully considered but they are not persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Election/Restrictions***

This application contains claims 6 and 12-57 drawn to an invention nonelected with traverse in the reply filed on 6-18-07. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 1-4 and 7-10 are under consideration as they relate to decreasing PGC numbers/development using DAZL proteins.

### ***Priority***

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

### ***Specification***

The amendment to Table 1 has been entered.

### ***Claim Rejections - 35 USC § 112***

#### ***Enablement***

I. Claims 1-4 and 7-10 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in

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the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 1 is drawn to a method for modulating primordial germ cells (PGC) numbers in an avian embryo, the method comprising immunizing a female bird with an antigen associated with primordial germ cells, whereby an egg produced by the female bird comprises a sufficiently high concentration of antibodies specific for the antigen to decrease endogenous PGC numbers in an avian embryo present within in the egg.

Claim 7 is drawn to a method for modulating primordial germ cells (PGC) development in an avian embryo, the method comprising immunizing a female bird with an antigen associated with primordial germ cells, whereby an egg produced by the female bird comprises a sufficiently high concentration of antibodies specific for the antigen to inhibit development of PGCs in an avian embryo present within in the egg.

The only purpose for the method claimed is to repopulate the treated embryo with donor PGCs from a different strain or species of avian to make a chimeric avian. The specification does not provide a use for the method claimed without making a chimeric avian.

The specification teaches decreasing PGC numbers in an embryo using DAZL-C and DAZL-N proteins administered to female chickens (pg 55, lines 19-26; pg 56, lines 12-17). The number of PGCs was determined by sacrificing the embryo (pg 54, lines 4-6). The specification does not teach an enabled use for these embryos without repopulating the embryo with donor PGCs.

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The specification suggests repopulating germ cells in treated embryos by injecting PGCs into the blood of stage 14-17 treated embryos (pg 57, lines 7-14). The specification suggests assessing the number of donor PGCs that repopulate the gonad of the recipient embryos (pg 57, lines 16-28).

The art is silent regarding treating an avian embryo to decrease PGC numbers/development and repopulating the treated embryo with donor PGCs from a different strain or species of avian to make a chimeric avian.

Applicants fail to teach how to determine whether PGC numbers had decreased in ovo without sacrificing the embryo. Specifically, applicants fail to teach how to determine whether amounts of antigens or antibodies that decrease endogenous PGC numbers had been injected or obtained as claimed without sacrificing the embryo. Survival of the embryo is essential to making a chimeric avian - the sole disclosed use for the method claimed. The specification fails to teach how to use the assay on pg 54 to determine the amounts of antigen or antibodies required to decrease endogenous PGC numbers without sacrificing the embryo. Furthermore, it is not readily apparent how to determine the values of antigens or antibodies required to decrease PGC numbers as claimed using the assay on pg 54 such that a chimeric avian could be made. Without such guidance, the specification has left those of skill with undue experimentation to determine how to decrease PGC numbers in an avian embryo as claimed without sacrificing the embryo.

The absence of how to repopulate PGCs in an embryo in the art and the lack of correlative evidence in the specification fails to enable the method claimed. The

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specification fails to overcome the absence in the art by reasonably teaching injecting donor PGCs into a treated embryo will repopulate the treated embryo to produce a viable chimeric avian. Merely injecting donor PGCs (pg 57, lines 10-14) and assessing PGC repopulation as suggested (pg 57, lines 16-28) is inadequate to indicate PGCs would successfully repopulate the embryo in which PGCs had been destroyed or that a viable avian would be obtained. It is not readily apparent from the specification that donor PGCs will target the proper position in the embryo to successfully replace the PGCs destroyed by the treatment so that a viable chimeric avian will be obtained. If the method described does not produce viable chimeras, it would require those of skill undue experimentation to determine how to fix the problem because the specification provides no additional suggestions. Accordingly, the claims are not enabled for its sole intended use; decreasing PGC numbers in an avian embryo for the purpose of repopulating the embryo with donor PGCs and obtaining a viable chimeric avian.

Upon overcoming the rejection above, the claims will have to be limited to using the elected species of DAZL antigen.

### **Response to arguments**

Applicants argue the claims as written are enabled for decreasing PGC numbers or development in an avian embryo. Applicants argue the avian embryos do not have to be used to repopulate the treated embryo with donor PGCs from a different strain or species of avian to make a chimeric avian. Applicants' argument is not persuasive. The rejection is based on how to use the method for its sole intended use - to deplete the PGCs in the avian embryos so they could be repopulated with donor PGCs from a

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different strain or species of avian to make a chimeric avian. The specification fails to enable those of skill to use the method claimed to make chimeric avians. As each claim must have at least one enabled use, merely depleting avian embryos in and of itself does not have an enabled use without repopulating the avian embryo with other PGCs. Therefore, the sole disclosed use must be considered under enablement.

Applicants argue pg 34, lines 19-26, teaches another use for decreasing PGC numbers in avian embryos. Applicants' argument is not persuasive. The citation is limited to using donor PGCs from a different strain or species. Nowhere is it explicitly or implicitly taught that the donor PGCs are the same species as the avian embryo.

"In particular embodiments of the presently disclosed subject matter, the number of endogenous PGCs in the recipient bird is reduced prior to introduction of the donor PGCs. In this manner, the donor PGCs can repopulate the gonads of the recipient bird and can increase the efficiency of producing chimeric birds and the proportion of gametes (and offspring) that are derived from the donor bird."

Applicants argue pg 42 teaches another use for decreasing PGC numbers in avian embryos. Applicants' argument is not persuasive. The citation is limited to increasing PGCs in an avian embryo and has nothing to do with the method now under consideration which is limited to decreasing PGCs in an avian embryo. Nowhere is it explicitly or implicitly taught on pg 42 that the decreasing PGCs in an avian embryo as claimed can be used to alter the sex ratio of embryos.

Applicants argue the sole intended use is enabled because the specification and the art at the time of filing taught that PGCs could be transferred to avian embryos. Applicants' argument is not persuasive. The specification and the art at the time of filing

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did not provide adequate guidance that PGCs from another strain or species of avian could repopulate an avian embryo in which the method claimed had been performed.

Applicants point to Example 3. Applicants' argument is not persuasive. Example 3 suggests repopulating germ cells in treated embryos by injecting PGCs into the blood of stage 14-17 treated embryos (pg 57, lines 7-14) and assessing the number of donor PGCs that repopulate the gonad of the recipient embryos (pg 57, lines 16-28). The absence of how to repopulate PGCs in an embryo in the art and the lack of correlative evidence in the specification fails to enable the method claimed. The specification fails to overcome the absence in the art by reasonably teaching injecting donor PGCs into a treated embryo will repopulate the treated embryo to produce a viable chimeric avian. Merely injecting donor PGCs (pg 57, lines 10-14) and assessing PGC repopulation as suggested (pg 57, lines 16-28) is inadequate to indicate PGCs would successfully repopulate the embryo or that a viable avian would be obtained. It is not readily apparent from the specification that donor PGCs will target the proper position in the embryo to successfully replace the PGCs destroyed by the treatment so that a viable chimeric avian will be obtained.

Applicants' arguments regarding the teachings in the art are noted but are not persuasive. While the art taught injecting PGCs into normal embryos with normal numbers of PGCs, the art did not teach how to do so in embryos in which PGC numbers or development had been inhibited as claimed. Merely injecting donor PGCs (pg 57, lines 10-14) into embryos in which PGC numbers/development had been inhibited, then assessing PGC repopulation as suggested (pg 57, lines 16-28) is inadequate to indicate

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PGCs would successfully repopulate the germ tissue or that a viable avian would be obtained. It is not readily apparent from the specification that donor PGCs would target the proper position in the embryo to successfully replace the PGCs decreased/inhibited by the treatment so that a viable chimeric avian will be obtained. If those of skill tried the suggestions in the specification and failed to produce viable chimeras, they would be left with undue experimentation to determine how to fix the problem - the specification provides no additional suggestions. Applicants do not point to teachings in the references repopulating an avian embryo with PGCs, where the embryo had decreased endogenous PGC numbers, which is the basis of the rejection.

### ***Indefiniteness***

II. Claims 1-4 and 7-10 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. The metes and bounds of what applicants consider “sufficiently high concentration of antibodies specific for the antigen to decrease the PGC numbers [or development] in an avian embryo” (claims 1 and 7) remain unclear. The concentration of antibodies required to decrease the number or development of PGCs is not set forth in the specification or the art at the time of filing. Accordingly, those of skill would not be able to determine when the concentration of antibodies obtained was infringing on the claim.

### **Response to arguments**

Applicants argue the “sufficiently high concentration of antibodies” is described functionally and that the rejection does not follow the framework for 112/2<sup>nd</sup> rejections. Applicants argue those of skill would understand how to determine whether PGC numbers decreased by reviewing the specification. Applicants’ arguments are not persuasive. The specification does not teach how to determine whether PGCs numbers decrease without sacrificing the avian (pg 54, lines 4-6, “Stage 27 (H&H) embryos were sacrificed”). The specification does not teach how to use the assay on pg 54 when making chimeric avians (the sole disclosed use for the method claimed). Accordingly, the specification fails to teach those of skill how to determine whether the amount of antibodies were “sufficiently high concentration” to decrease PGC numbers, such that the avian embryo could then be injected with donor PGCs. Without such guidance, those of skill using the method to make a chimeric avian would not be able to determine when “sufficiently high concentrations” of antibodies had been obtained.

Furthermore, the examiner is not asking for a unique value of antibody concentrations. Applicants fail to teach how to determine whether PGC numbers had decreased in ovo (without sacrificing the embryo) and fail to teach the amounts of “sufficiently high concentrations of antibodies” that decrease endogenous PGC numbers. The disclosure is silent in both regards. It is not readily apparent how to determine the values of antibodies required to decrease PGC numbers as claimed.

The framework of the rejection is correct because it is based on the lack of teachings in the specification regarding how to determine whether functional amounts of

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antibodies had been obtained in an embryo without sacrificing it, which is essential to the invention.

B. The metes and bounds of what applicants consider antibodies “specific for the antigen to decrease endogenous PGC numbers” (claims 1 and 7) are unclear. The phrase, “to decrease endogenous PGC numbers” is an intended use that may not occur. It cannot be determined how specific the antibodies must be to decrease endogenous PGC numbers. The specification and the art at the time of filing provide no guidance in this regard. Accordingly, those of skill would not be able to determine whether antibodies that recognized any DAZL antigen, for example, was encompassed by the claim of if the phrase was limited to antibodies that are specific to a particular DAZL antigen, i.e. DAZL-C or DAZL-N.

### **Response to arguments**

Applicants argue the examiner is basing the rejection on functional language without interpreting the language in context of the claim as one of ordinary skill in the art. Applicants’ argument is not persuasive. The specification and the art do not teach how specific the antibodies must be to the antigen to decrease PGC numbers.

Applicants argue the language relates to an outcome – the decrease in PGCs. Applicants’ argument is not persuasive. As written, the outcome is not directly linked to the antigen or the antibodies. The claims are not limited to administering antigens to an avian embryo, wherein the antigens are specific to avian PGCs, such that endogenous PGC numbers in the avian embryo decrease. The claims are not limited to administering an antigen to an avian embryo, such that antibodies that recognize the

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antigen are obtained, wherein the amount of antibodies obtained are sufficient to decrease endogenous PGC numbers in the avian embryo. As written, it is unclear how the specificity of the antibodies to the antigen relates to the outcome.

The art did not reasonable teach or suggest modulating primordial germ cells (PGC) numbers/development in an avian embryo by immunizing a female bird with an antigen associated with primordial germ cells, whereby an egg produced by the female bird comprises a sufficiently high concentration of antibodies specific for the antigen to decrease the number of PGCs or inhibit the development of PGCs in an avian embryo present within in the egg.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Wilson who can normally be reached at the office on Monday, Tuesday, Thursday and Friday from 9:30 am to 6:00 pm at 571-272-0738.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517.

The official fax number for this Group is (571) 273-8300.

Michael C. Wilson

/Michael C. Wilson/  
Patent Examiner